

REMARKS

This amendment moots the rejection of claim 90 vis-à-vis reference to the tables (point 5 on page 6 of the November 7, 2007 action) and the related June 11, 2008 holding of non-responsiveness vis-à-vis the use of tables in claims 43 and 90. (A petition challenging the holding of non-responsiveness was filed on even date herewith.) The examiner, in the November 7, 2007 office action, apparently overlooked the use of tables in claims 90 and 92, but for the sake of completeness we address those claims, too.

Since a simple reference to the tables is insufficient to properly protect applicant's invention, we have amended claims 43, 90, 91 and 92 to avoid reference to tables. Instead, these claims now explicitly recite appropriate choices for R1 and, in the case of claims 90 and 92, for R2 and R3.

We have indicated the insertion of the formulae, as required by 37 CFR 1.121, by underlining. The formulae are provided in "blocks" of several formulae and each block is underlined.

Please note that claims 90 and 92 do end, as required by PTO practice, with a period. It is immediately after the R3 formula, at the left margin.

In present claim 43 it is stated that "wherein R1 is the side chain of an amino acid selected from the group consisting of *amino acids mentioned in tables 1, 2, 3, 7 and 9*". As the tables contains various compounds used to synthesize the libraries of the invention, such as, e.g., spacers, linkers, encoding tags, reagents, and amino acid building blocks, and therefore not only amino acids, the relevant content of the tables, i.e. the amino acids, have been extracted for incorporation into the claims.

Accordingly, among the compounds of table 1, compound PLL (1) and compound (2) were omitted as they are not amino acid

building blocks but linker and spacer, respectively. Basis for this can be found at page 73, at line 20, and at lines 23-24.

Among the compounds of table 2, compounds 36, 37 and 38 were removed as they are not amino acid building blocks but aliphatic encoding tags. Basis for this can be found at page 77, lines 5-6.

Among the compounds of table 3, compounds 49-52 were omitted as they are not amino acid building blocks but amino aldehydes. This will be evident to a skilled person within the field of organic chemistry, as the compounds do not contain an acid group. Compound 53 was furthermore omitted because it is not an amino acid but a reagent.

Among the compounds of table 7, compounds 54, 55a, 55b, and 63 were omitted as they are not amino acid building blocks but linkers and spacers. Basis for this can be found at page 110, line 7, page 110, line 11 (azido-PEG-amine), page 118, lines 16-17 (O-(N-Fmoc-2-aminoethyl)-O-(2-carboxyethyl)-undecaethylenglycol), and page 108, line 8, respectively. Compounds 56 - 62, and 77 - 81 were omitted because they are not amino acid building blocks but esters, acids, acid chlorides, ketones or amines. This will be evident to a skilled person within the field of organic chemistry.

Among the compounds of table 9, compounds 107-126 were omitted as they are not amino acid building blocks but rather aldehydes, amino aldehydes, ketones, acid chlorides or other acids. This will be evident for a skilled person within the field of organic chemistry.

The tables as originally filed cited compounds to be used directly in the synthesis of libraries, therefore the compounds were shown carrying protective groups as appropriate for the different synthetic steps applied. The protective groups may e.g. be present at amino acids, such as at the alpha amino group of the amino acid and at the side chains if relevant for the specific amino acid in question. The person

skilled in the art will recognize from his general knowledge within the field, together with the examples given in the application, that final compounds of formula IV do not carry these protective groups. Therefore the protective groups have been removed from the amino acids that are to be directly incorporated into the claims. Further support and enablement for the removal of protective groups will be described below.

Tables 1, 2, 3, 7 and 9 contain amino acids that may be protected at the alpha amino group of the amino acid; this option is marked by a R₁ group at the amine. Kindly note that this R₁ group does not refer to the R1 group of formula IV. For example in table 1, page 53, it is stated that R₁ is either Fmoc, Boc or H, this is likewise stated generally for the tables and schemes at page 52, line 9. For the amino acids adapted for incorporation in the claims, this R₁ group has been replaced with H, i.e. unprotected amino acid.

Tables 1, 2, 3, 7 and 9 further contain amino acids where the side chains contains groups that for synthesis purposes are protected by one of the following: i) an alcohol or carboxylic acid protecting group, tert-butyl (tBu), ii) an amine protecting group, tert-butyl carbamate (Boc), iii) an amine protecting group, trityl (Trt), iv) an alchohol protecting group, acetyl (Ac), and v) guanidine protecting group, 2,2,5,7,8-pentamethylchromane-6-sulfonyl (Pmc). For the amino acids adapted for incorporation into the claims, these protecting groups has been removed, so as to more clearly show the possibilities for R1 side chains in final compounds of formula IV.

Support and enablement for the removal of these protecting groups can be seen from the Examples of the present invention, specific references to the Examples are given below here.

- i) The alcohol or carboxylic acid protecting group, tert-butyl (tBu), as e.g. in compounds **5**, **9**, **16** and **26**, or as in compounds **6**, **9** and **17**, repectively, can be removed by treatment with 85% TFA containing 2% triisopropylsilane, 2.5% EDT, 5% thioanisole, 5% water for 1 hour. This deprotection step is exemplified at page 74, lines 16-18, where it is stated that acid labile protection groups were removed in this manner. It will be well-known to a person skilled in the art that a tBu group is an acid labile protective group.
- ii) The amine protecting group, tert-butyl carbamate (Boc), whether on the alpha amino group or on the amine side chains as e.g. in compounds **8**, **10**, **11**, **25**, **39**, **40**, **42**, and **43** can be removed by treatment with 85% TFA containing 2% triisopropylsilane, 2.5% EDT, 5% thioanisole, 5% water for 1 hour. This deprotection step is exemplified at page 74, lines 16-18, where it is stated that acid labile protection groups were removed in this manner. It will be well-known to a person skilled in the art that a Boc group is an acid labile protective group. Alternatively, the Boc group can be removed by treatment with 10% TFA in DCM (dichloromethane). This type of deprotection is exemplified at page 76, lines 1-2.
- iii) The amine protecting group, trityl (Trt), as in compound **10**, **18** and **19** can be removed by treatment with 85% TFA containing 2% triisopropylsilane, 2.5% EDT, 5% thioanisole, 5% water for 1 hour. This deprotection step is exemplified at page 74, lines 16-18, where it is stated that acid labile protection groups were removed in this manner. It will be well-known to a person skilled in the art that a Trt group is an acid labile protective group.
- iv) The alcohol protecting group (e.g. at carbohydrate -OH), acetyl (Ac), as in compounds **32**, **33**, **34** and **35** can be removed

by treatment with hydrazine hydrate in methanol for 6 hours. This deprotection step is exemplified at both page 76, lines 2-4, and page 77, lines 24-26, where it is stated that carbohydrate acetyl protecting groups were removed by hydrolysis in this manner.

v) The guanidine protecting group, 2,2,5,7,8-pentamethylchromane-6-sulfonyl (Pmc), as in compound **48** can be removed by treatment with a cocktail comprising TFA 87.5%, EDT 2.5%, thioanisole 5% and H₂O 5% for 2.5 hours. This is exemplified at page 77, lines 20-21.

Claims 43 and 91 thereby recite, as choices for R1, the "deprotected" forms of the following compounds:

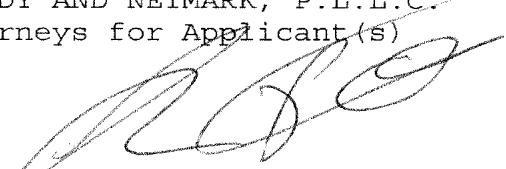
from table 1: 3-20
from table 2: 21-35
from table 3: 39-48
from table 7: 64-76
from table 9: 103-106, 127, 128.

In like manner, claims 90 and 92 now recite only the deprotected amino acids of the previously cited tables as choices for R1, R2 and R3. For R1, we have deprotected compounds 3, 4, 12, 13, 15, 20, 21, 23, 23, 24, 28, 29, 31, 47, 64, 66, 67, 71, 73, 74, 103, 104, 105, 106 and 128. For R2, we have deprotected compounds 117-126. For R3, we have deprotected compounds 103-116 and 128.

USSN - 10/541,501

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